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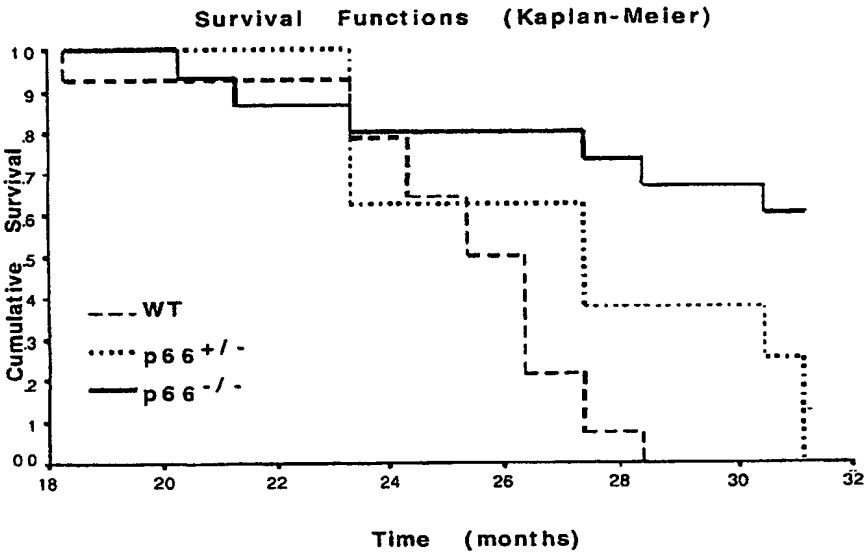

(57) Abstract

It has been determined that i) $p66^{shc}$ is serine phosphorylated upon UV treatment or oxidative damage; ii) the serine–phosphorylation of p66 by oxidative signals is mediated by Erk1 and p38, as shown both in vivo and in vitro; iii) ablation of $p66^{shc}$ expression by homologous recombination enhances resistance to oxidative damage both *in vitro* and *in vivo*; iv) a serine–phosphorylation defective mutant of $p66^{shc}$ is unable to restore a normal stress response in $p66^{shc}$ targeted cells; v) mice carrying the $p66^{shc}$ targeted mutation have prolonged lifespan.